EXHIBIT 32

REMARKS

Applicants respectfully request reconsideration and withdrawal of the outstanding rejections. For at least the reasons stated below, the outstanding Official Action fails to present a *prima facie* case of obviousness. Thus, Applicants traverse the rejections, and urge reconsideration and withdrawal of all outstanding rejections. Applicants present this Response together with a Request for Continued Examination and the appropriate fee, and so it is urged that these amendments and remarks are entitled to entry and due consideration.

By this amendment, claims 34, and 73-75 have been canceled, without prejudice or disclaimer. Claim 72 has been amended to add the limitation that the content of binding cellulose derivative in the claimed method represents from 5 to 12% by weight of the combined neutral core, and the fenofibrate, surfactant and binding cellulose derivative of the active layer.

Claims previously interposed in this case (e.g., claim 34), and in related cases, have been directed to methods using similar formulations but wherein the binding cellulose derivative is 2 - 15% by weight of the composition. In the instant case, original claim 12 recited that the binding cellulose derivative is 5 to 12% by weight of the formulation. Thus, the limitation is supported by the application as filed.

Claim 72, and its dependent claims, now recites a method for reducing food effect using a pharmaceutical composition having a weight ratio of fenofibrate to binding cellulose derivative of 5/1 to 15/1, and wherein the binding cellulose derivative is 5 to 12 % by weight of the combined neutral core, and the fenofibrate, surfactant and binding cellulose derivative of the active layer. Neither of those

limitations were taught or suggested by the prior art, and, when taken together, the dual limitation clearly distinguishes over the prior art.

In addressing Applicants' previously presented arguments, the Advisory Action asserts that the Stamm reference teaches or suggests the claimed invention. Applicants respectfully disagree. The Advisory Action misconstrues and mischaracterizes the Stamm reference, and likewise mischaracterizes applicant's response.

In restating the Office position with regard to Stamm, the Advisory Action states that "While Applicant agrees with the rationale set forth in the action, Applicant insist that there is no prima facie case…." To avoid any confusion on the record, Applicants wish to clarify that they agree with the latter, but not the former. Applicants do not concede any rationale of the prior office action, but do maintain that the rejections fail to make a prima facie case.

The Stamm reference continues to be misrepresented and mischaracterized. The Stamm reference does not "teach a pharmaceutical composition comprising micronized fenofibrate, a surfactant, and a binder, of a cellulose derivative such as hydroxymethylpropylmethylcellulose [*sic*] wherein the hydrophilic polymer is from 5 - 40% by weight *in a granular form*." (citations omitted).

The cited text is quite clear that Stamm is speaking of a fundamentally different composition - a starting material that is a *suspension* of the active ingredient. Col. 6, lines 17-21 ("The significant starting product is the *suspension* of the active ingredient. This *suspension* is prepared by putting the micronized active ingredient into *suspension* in a solution comprising the hydrophilic polymer and, optionally, a surfactant, in solution in a solvent." emphasis added). The passage

relied upon in the rejection specifically states "The hydrophilic polymer concentration *in the suspension* is from 5 to 40% by weight, preferably 10 to 25%." Col. 6, lines 36-37 (emphasis added). Thus, the hydrophilic polymer is present at 5-40% by weight *of the suspension*, which necessarily includes the solvent.

The suspension is sprayed onto inert cores by various means to form granules. *See, e.g.,* Col. 5, lines 31-67. One skilled in the art would immediately appreciate that spraying the suspension onto the inert cores to form granules necessarily involves drying the suspension by removal of the solvent. Removal of the solvent changes the relative concentration of the hydrophilic polymer; and particularly *relative to the resulting granular form of the pharmaceutical composition.* Once the granular form of the pharmaceutical composition is formed, the relative concentration of hydrophilic polymer is no longer 5-40%. Indeed, without more, it would have been impossible to know what the relative concentration of hydrophilic polymer would be in the resulting pharmaceutical composition. However, Stamm's specification provides that information explicitly. It states that, relative to the pharmaceutical composition (not the suspension), the hydrophilic polymer represents "from 20 to 60% by weight, preferably 25 to 45% by weight...." Col. 5, lines 4-6; *see also,* col. 5, lines 11-12 ("The hydrophilic polymer represents preferably more than 25% by weight, based on the weigt [*sic*] of (a)."). Thus, Stamm teaches that a sufficient amount of the *suspension* is used to coat the neutral core such that one arrives at a pharmaceutical composition having *at least* 20%, and preferably *more than 25%*, by weight of the hydrophilic polymer.

The Stamm reference itself makes it abundantly clear that the concentration of the hydrophilic polymer relative to the granular pharmaceutical composition as a whole is not 5-40%; but rather is from 20-60%.

Stamm, when properly considered for all that it would have taught one of skill in the art, squarely teaches away from the claimed invention by stating that the preferred amount, and hence the direction for optimization, is away from the direction Applicants have gone. Applicants' claims are directed to methods using a formulation wherein the hydrophilic polymer relative to the finished pharmaceutical composition is 5-12% by weight - less than half the amount Stamm teaches is preferred. Thus, Stamm does not teach or suggest the claimed invention. Reconsideration and withdrawal of the rejection, insofar as it relies upon Stamm, is appropriate, and earnestly solicited.

Finally, Stamm also teaches that "The weight ration [*sic*] fenofibrate/hydrophilic polymer can for example be comprised between 1/10 and 4/1, preferably, for example, between 1/2 and 2/1." Col. 5, lines 13-15. Stamm again teaches that the preferred formulations are those wherein the quantity of hydrophilic polymer, relative to fenofibrate, is best when at the higher end of the range with greater quantities of hydrophilic polymer. In contrast, the claimed invention specifies a pharmaceutical composition having a ratio not merely outside that range, but one where the ratio favors less, rather than more, of the hydrophilic polymer, i.e., from 5/1 to 15/1. The claimed invention is thus one where the fenofibrate/hydrophilic polymer ratio is substantially greater, reflecting a formulation of significantly lower quantities of hydrophilic polymer than those of Stamm.

Even if the art were to have motivated a worker to explore modifying the fenofibrate/hydrophilic polymer ratio in an effort to reduce the food effect, a premise Applicants reject, the Stamm reference would have led such a worker toward more - not less - hydrophilic polymer. Accordingly, there is no prima facie case of obviousness based on Stamm, either alone or in combination; and reconsideration and withdrawal of the rejection is requested.

Applicants wish to emphasize that the claimed invention is not merely a reduction in food effect of fenofibrate formulations. That is something the art has been striving toward for some time. However, the art fails to teach or suggest any claimed means for doing it. The claimed method involves, among other things, use of a formulation wherein a neutral core is coated with an active layer of fenofibrate, hydrophilic polymer, and surfactant; and wherein the hydrophilic polymer represents a 5-12% by weight of the composition; and the weight ratio of fenofibrate/hydrophilic polymer is 5/1 to 15/1. Applicants' specification and supporting evidence submitted in this and related cases show that the prior art has thus far been unsuccessful at achieving the consistent high level of bioavailability of the claimed formulation regardless of the diet of the patient.

As the Official Action and subsequent Advisory Action correctly note, the art recognized that certain active agents suffer a food effect, and that the elimination of the food effect is of great interest to those working in the field. However, none of the cited references teaches or suggests how that food effect can be eliminated. Moreover, none teaches or suggests the claimed method. By the express reasoning of the rejection, the art has acknowledged that fenofibrate in particular suffers low bioavailability, and has an associated food effect. The rejection acknowledges the

art recognition that this food effect of fenofibrate is a longstanding problem. The cited art, however, fails to provide an effective solution to the acknowledged food effect; and, particularly, fails to teach or suggest the claimed method. This long sought, but unsolved need, is a persuasive indicator of non-obviousness, and must be taken into consideration in assessing patentability under 35 USC § 103.

Additionally, and as argued, the remaining references fail to teach or suggest the claimed invention, alone or in combination with Stamm.

Curtet teaches pharmaceutical compositions containing fenofibrate co-micronized with a solid surfactant. Stamm disparages co-micronized formulations as inadequate to improve bioavailability. As the two references are at odds over various features, including co-micronization, the skilled worker would *not* have been motivated to combine the teachings of Curtet and Stamm; and, even if one were so motivated, there has been no showing that one would have arrived at the claimed invention.

Curtet does not teach the use of a neutral microgranule, but rather teaches a wet granulated mixture. *See, e.g*, Curtet, column 2, lines 5-20. Nothing in Curtet teaches or suggests the use of a neutral microgranule. If, however, one were to look to Stamm for that teaching, there is no showing that one would have arrived at the claimed invention. That is, the skilled worker would have had to choose from the various alternatives presented by the two references, without any demonstrable guidance as to which of the various options to choose, and then somehow arrive at the claimed invention. To support the *prima facie* case of obviousness, the rejection must show how or why the ordinary skilled worker would have been motivated to choose the actual variables now claimed from those two references so as to arrive at

the claimed invention. No such showing has been made. Indeed, the rejection is nothing more than a hindsight reconstruction of the claimed invention using the instant claims as a template without regard to what the references themselves teach. Accordingly, there is no *prima facie* case, and the rejection must be withdrawn.

Finally, Applicants invite the Office's attention to related U.S. Patent No. 7,101,574, as to which Applicants have submitted a Terminal Disclaimer. The claims of the '574 patent are directed to a distinct yet analogous invention. There, as here, the claims include reference to a pharmaceutical composition in the form of granules having an active layer coating a neutral core. The active layer has a specified concentration of fenofibrate relative to the pharmaceutical composition; and a specified concentration of hydrophilic polymer relative to the pharmaceutical composition. The claims of the '574 patent, however, are directed to pharmaceutical compositions, per se, and to specific methods of making those compositions.

The instant claims are distinct in that they are directed to a method of reducing food effect; and the pharmaceutical composition used in that method uses distinct concentration ranges of fenofibrate and hydrophilic polymer, and expresses those ranges in alternative units.

To the extent that the instant claims are similar to those of the '574 patent, they are nonetheless patentably distinct and patentable as they recite differing ranges. Further, Applicants' duly executed Terminal Disclaimer eliminates any associated double patenting issues. Accordingly, as with the '574 patent, the instant claims are patentable over the art, and reconsideration and withdrawal of all outstanding rejections is respectfully requested.

Conclusion

In view of the foregoing amendments and remarks, applicants respectfully request reconsideration and withdrawal of all outstanding rejections. Applicants submit that the claims are now in condition for allowance, and respectfully request formal notification to that effect. If, however, the Examiner perceives any impediments to such a notice of allowability, whether substantive or formal, the Examiner is encouraged to call Applicants' attorney at the number provided below. Such informal communication will expedite examination and disposition of this case.

Respectfully submitted,

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